HFI-35

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
6751 Steger Drive
Cincinnati, OH 45237-3097

M3958n

July 14, 2000

WARNING LETTER
CIN-WL-00-2122

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Dr. Praful R. Patel, President
National Biochemicals Corp.
1632 Enterprise Parkway
Twinsburg, OH 44087

Dear Dr. Patel:

The Food and Drug Administration conducted an inspection of your bulk drug repackaging and distribution facility, located in Twinsburg, Ohio, on February 22 –24, 28, 29 and March 2, 2000. This inspection determined that you are repackaging and distributing bulk active pharmaceutical ingredients (APIs), which are in violation of Sections 502(f)(1) and 502(o) of the Federal Food, Drug, and Cosmetic Act (the Act).

Section 502(f)(1) of the Act requires that drugs bear adequate directions for use. Because they will undergo further processing prior to use, bulk drugs may be exempted from this "adequate directions for use" requirement if they meet the conditions established in Title 21, Code of Federal Regulations, Section 201.122 (21 CFR 201.122). As stated in 21 CFR 201.122, APIs used to produce new animal drugs are exempt from the requirement for adequate directions for use under 502(f)(1) if used to produce an animal drug that is covered by an approved new animal drug application. Conversely, an API that is used to produce an unapproved new animal drug is not exempt from the requirement for adequate directions for use and is therefore misbranded under 502(f)(1).

Several of the bulk active pharmaceutical ingredients sold by your firm are not entitled to this exemption. As stated in the regulations, the exemption does not apply to a substance intended for use in manufacture, processing or repacking a new animal drug, unless the finished drug is covered by an approved application, and the API is delivered to the holder of the approved application.

We recognize that there may be some end uses for bulk chemicals that may not be regulated by FDA. Other uses, such as human drug compounding, may be legal when performed in accordance with the Food and Drug Administration Modernization Act (FDAMA). In contrast, most compounded animal drugs are illegal because they are unapproved new animal drugs. As a matter of regulatory discretion, the Food and Drug Administration may not institute legal action against the compounding of some new animal drugs when the situation is "of great need and small risk", (Compliance Policy Guide 608.400, "Compounding Drugs for Use in Animals"). However, this policy does not apply to use of APIs in compounding drugs for use in "food producing animals", nor does it apply to their use in medicated feeds. These uses may introduce a significant risk for unsafe drug residues in edible tissues.

You should also be aware that your API products are not exempted under the extra-label drug use provisions of the Animal Medicinal Drug Use Clarification Act, (AMDUCA). The implementing regulations for AMDUCA, 21 CFR 530.1, states "This part applies to the extralabel use in an animal of any approved new animal drug or approved new human drug..." **Your APIs are not approved drugs.** 21 CFR 530.11(b) prohibits extralabel use of drugs in or on an **animal feed**. 21 CFR 530.13(a) states "nothing in this part shall be construed as permitting compounding from bulk drugs." In summary, provisions and exemptions for **extra-label drug use do not apply to feeds, APIs or unapproved drugs.**

We recognize that our Compliance Policy Guide tolerating some compounding of unapproved new animal drugs and the human drug compounding provisions of FDAMA make it more difficult for API distributors to assess the legality or acceptability of the use of these drugs. Nevertheless, you must make this assessment. We recognize that you have made some attempts to establish the intended uses for these APIs. However, your efforts appear to be totally inadequate. On at least one occasion you determined that an API would be used in food producing animals, yet you failed to act on this information and shipped the drug anyway. For other drugs, you either did not have information on their intended use or you had inadequate information to determine the legality of their use. Neither situation is acceptable.

The regulation, 21 CFR 201.150, requires a written agreement between API shippers and recipients, assuring that the APIs will not be adulterated or misbranded by the end users. National Biochemicals did not have such assurance. In fact, you had information to the contrary. You were told by one customer, [redacted], that the API (Penicillin G Procaine) you sold to him was to be used to make a feed for treatment of pneumonia in swine. Several other of the bulk APIs, distributed by your firm, also appear to have been used or intended for use to make unapproved new animal drugs for food animals. You are responsible, as a distributor of bulk animal drugs (APIs), which do not bear adequate directions for use, for assuring that the drugs being produced are covered by an exemption or an approved application before they are shipped. Distributors will be held accountable when drugs (APIs) they sell are used to manufacture unapproved drug products and they have not taken proper steps to prevent such illegal use.

Bulk API drug products repackaged by your firm are also misbranded under Section 502(o) of the Act in that they were packaged in an establishment not duly registered under Section 510 of the Act, and the drugs have not been listed as required by Section 510(j). You were previously warned in Warning Letter CIN-WL-96-532, dated December 24, 1996, that you had failed to file a Drug Establishment Registration and Drug Product Listings. Your January 10, 1997 response to the 1996 Warning Letter indicated you had filed a Drug Establishment Registration with FDA and were in the process of completing your Drug Product Listings. During the subsequent inspection of August 26-28, 1997, you informed our investigators that you were no longer repackaging or relabeling drugs. During the current inspection, you again indicated that you were only a distributor and were no longer repackaging drugs. However, our FDA Investigators found evidence during the current inspection that you continue to repackage API drug products. When you were informed of this, you told our investigators that you were not aware that your employees were repackaging drug products and that this repackaging was unauthorized.

You should be aware that you are responsible for assuring that your firm operates in compliance with the law. Should you continue your repackaging or relabeling operations, you must register your firm as a Drug Establishment, list your drug products, and fully comply with the applicable Good Manufacturing Practice regulations, including the establishment of appropriate written procedures and batch production records.

The above is not intended to be an all-inclusive list of violations. As a repacker and distributor of active pharmaceutical ingredients, you are responsible for assuring that your overall operation and the products you repackage and distribute are in compliance with the law.

You should take prompt action to correct these violations and to establish procedures to prevent their recurrence. Failure to promptly correct these violations may result in regulatory action without further notice, such as seizure and/or injunction.

You should respond to this office within fifteen (15) working days of receipt of this letter of the additional steps taken to correct these violations, including an explanation of each step taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. You reply should be sent to Charles S. Price, Compliance Officer, at the above address. If you have any questions, you may call Mr. Price at (513) 679-2700 extension 165.

Sincerely,

Henry L. Fielden
Director,
Cincinnati District Office